

## WHAT IS CLAIMED IS:

1. A method for the treatment of psychiatric disorder in a patient, said method comprises administering to said patient a therapeutically effective amount of a PDE4 inhibitor in combination with psychotherapy.

2. The method of Claim 1 wherein said psychiatric disorder is posttraumatic stress disorder.

3. The method of Claim 1 wherein said psychotherapy is selected from behavior psychotherapy, cognitive psychotherapy, and psychodynamically oriented psychotherapy.

4. The method of Claim 2 wherein said psychotherapy is selected from behavior psychotherapy, cognitive psychotherapy, and psychodynamically oriented psychotherapy.

5. The method of Claim 1 wherein said psychotherapy is exposure-based psychotherapy.

6. The method of Claim 2 wherein said psychotherapy is exposure-based psychotherapy.

7. The method of Claim 1 wherein said psychotherapy is cognitive psychotherapy.

8. The method of Claim 2 wherein said psychotherapy is cognitive psychotherapy.

9. The method of Claim 1 wherein said PDE4 inhibitor is selected from cilomilast, roflumilast and roflumilast N-oxide.

10. The method of Claim 1 wherein said PDE4 inhibitor is selected from cilomilast, roflumilast and roflumilast N-oxide.

11. The method of Claim 1 or 2 wherein said PDE4 inhibitor is selected from the group consisting of:

6-isopropyl-8-(3-{(Z/E)-2-[4-(methylsulfonyl)phenyl]-2-phenylethenyl}phenyl)quinoline;

6-isopropyl-8-{3-[(E/Z)-2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]-

phenyl}quinoline;

6-isopropyl-8-(3-{(E)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}-phenyl)quinoline;

6-isopropyl-8-(3-{(Z/E)-2-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl]ethenyl}-phenyl)quinoline;

2-(2-{(E/Z)-2-[3-(6-isopropyl-8-quinolinyl)phenyl]-1-[4-(methylsulfonyl)phenyl]ethenyl}-1,3-thiazol-5-yl)-2-propanol;

2-[8-(3-{(E/Z)-2-[5-(1-hydroxy-1-methylethyl)-1,3-thiazol-2-yl]-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)-6-quinolinyl]-2-methylpropanenitrile;

2-methyl-2-[8-(3-{(E)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}-phenyl)-6-quinolinyl]propanenitrile;

6-[1-(methylsulfonyl)ethyl]-8-{3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]phenyl}quinoline;

6-[1-methyl-1-(methylsulfonyl)ethyl]-8-{3-[(E)-2-[4-(methylsulfonyl)phenyl]-2-(1,3-thiazol-2-yl)ethenyl]phenyl}quinoline;

8-(3-{(Z)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)-6-[1-(methylsulfonyl)ethyl]quinoline;

8-(3-{(Z)-2-(1-methyl-1H-imidazol-2-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)-6-[1-methyl-1-(methylsulfonyl)ethyl]quinoline;

6-[1-methyl-1-(methylsulfonyl)ethyl]-8-(3-{(E/Z)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)quinoline;

(E/Z)-3-{3-[6-(1-cyano-1-methylethyl)-8-quinolinyl]phenyl}-N-isopropyl-2-[4-(methylsulfonyl)phenyl]-2-propenamide;

8-(3-{(E)-2-{3-[(4-methoxyphenoxy)methyl]-1,2,4-oxadiazol-5-yl}-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)-6-[1-methyl-1-(methylsulfonyl)ethyl]quinoline;

(5-{(E)-2-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-1-[4-(methylsulfonyl)phenyl]ethenyl}-1,2,4-oxadiazol-3-yl)methanol;

(E)-N-isopropyl-3-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide;

(E)-3-{3-[6-(1-cyano-1-methylethyl)-8-quinolinyl]phenyl}-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid;

- 2-methyl-2-[8-(3-{(E)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}-phenyl)-6-quinolinyl]propanenitrile;
- (E)-3-{3-[6-(1-cyano-1-methylethyl)-8-quinolinyl]phenyl}-2-[4-(methylsulfonyl)phenyl]-2-propenamide;
- 5 (E)-N-(tert-butyl)-3-{3-[6-(1-cyano-1-methylethyl)-8-quinolinyl]phenyl}-2-[4-(methylsulfonyl)phenyl]-2-propenamide;
- (E)-3-[3-(6-isopropyl-8-quinolinyl)phenyl]-2-[4-(methylsulfonyl)phenyl]-2-propenoic acid;
- 6-isopropyl-8-(3-{(E)-2-(3-methyl-1,2,4-oxadiazol-5-yl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)quinoline;
- 10 (E)-3-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-2-[4-(methylsulfonyl)phenyl]-1-(1-pyrrolidinyl)-2-propen-1-one;
- (E)-N-cyclopropyl-3-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-2-[4-(methylsulfonyl)phenyl]-2-propenamide;
- (E)-N-(tert-butyl)-3-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-2-[4-
- 15 (methylsulfonyl)phenyl]-2-propenamide;
- 8-{3-[2,2-bis(4-chlorophenyl)vinyl]phenyl}-6-isopropylquinoline;
- 6-isopropyl-8-(3-{(E/Z)-2-(6-methyl-3-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl}-phenyl)quinoline;
- 6-isopropyl-8-(3-{(E/Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)quinoline;
- 20 8-(3-{2,2-bis[4-(methylsulfonyl)phenyl]vinyl}phenyl)-6-isopropylquinoline;
- 2-methyl-2-[8-(3-{(E/Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)-6-quinolinyl]propanenitrile;
- 2-[8-(3-{2,2-bis[4-(methylsulfonyl)phenyl]vinyl}phenyl)-6-quinolinyl]-2-methylpropanenitrile;
- 25 2-methyl-2-(8-{3-{(E)-2-[4-(methylsulfonyl)phenyl]-2-(2-pyridinyl)ethenyl}phenyl}-6-quinolinyl)propanenitrile;
- 6-[1-methyl-1-(methylsulfonyl)ethyl]-8-(3-{(E/Z)-2-(5-methyl-2-pyridinyl)-2-[4-(methylsulfonyl)phenyl]ethenyl}phenyl)quinoline;
- 2-(6-{(E)-2-(3-{6-[1-methyl-1-(methylsulfonyl)ethyl]-8-quinolinyl}phenyl)-1-[4-
- 30 (methylsulfonyl)phenyl]ethenyl}-3-pyridinyl)-2-propanol;
- (±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]-thiazolyl}ethyl}pyridine *N*-oxide;
- chiral 4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]-thiazolyl}ethyl}pyridine *N*-oxide;

- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-2,2,2-trifluoro)ethyl)-thiazolyl]ethyl}pyridine;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-2,2,2-trifluoro)-ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- 5 (±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-[2-(1-hydroxy-1-trifluoromethyl-2,2,2-trifluoro)ethyl]thiazolyl]ethyl}pyridine;
- (±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-[2-(1-hydroxy-1-trifluoromethyl-2,2,2-trifluoro)ethyl]thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-[2-(1-hydroxy-1-trifluoromethyl)ethyl]-thiazolyl]ethyl}pyridine *N-oxide*;
- 10 (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-phenylmethanol)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-phenyl)ethyl)-thiazolyl]ethyl}pyridine *N-oxide*;
- 15 (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-phenyl-2,2,2-trifluoro)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-phenyl)propyl)-thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-cyclohexylmethanol)-thiazolyl]ethyl}pyridine;
- 20 (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-cyclohexyl-2,2,2-trifluoromethyl)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(4-ethyl)phenyl)ethyl)-thiazolyl]ethyl}pyridine *N-oxide*;
- 25 (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(4-ethyl)phenyl-2,2,2-trifluoro)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(4-fluoro)phenyl)-ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(4-fluoro)phenyl-2,2,2-trifluoro)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- 30 (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(5-bromopyridin-2-yl)-2,2,2-trifluoro)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;
- (±/±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-[5-(2-(1-hydroxy-1-(6-bromopyridin-3-yl)-2,2,2-trifluoro)ethyl)thiazolyl]ethyl}pyridine *N-oxide*;

- (±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy)cyclobutyl]thiazolyl}-ethyl}pyridine *N*-oxide;
- (±)-4-{2-[3,4-Bis(difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy)cyclohexyl]thiazolyl}-ethyl}pyridine *N*-oxide;
- 5 (±)-4-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- chiral 4-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- (±)-4-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-trifluoromethyl)-2,2,2-trifluoroethyl]thiazolyl}ethyl}pyridine;
- 10 (±)-4-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-trifluoromethyl)-2,2,2-trifluoroethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- chiral 3-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine;
- 15 chiral 3-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- chiral 3-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- chiral 3-{2-[(3-cyclobutyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-trifluoromethyl)-2,2,2-trifluoroethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- 20 (±)-4-{2-[(3-cyclopropyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-methyl)ethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- (±)-3-{2-[(3-cyclopropyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-trifluoromethyl)-2,2,2-trifluoroethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- 25 chiral 3-{2-[(3-cyclopropyloxy-4-difluoromethoxy)phenyl]-2-{5-[2-(1-hydroxy-1-trifluoromethyl)-2,2,2-trifluoroethyl]thiazolyl}ethyl}pyridine *N*-oxide;
- N-Isopropyl-1-[3-(phenylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;
- N-Isopropyl-1-[3-(2-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-
- 30 carboxamide;
- N-Isopropyl-1-[3-(4-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;
- N-Isopropyl-1-[3-(1-oxido-4-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;
- 35 N-Isopropyl-1-(3-ethynylphenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

- N-Cyclopropyl-1-(3-ethynylphenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(1-oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
5 N-Cyclopropyl-1-[3-(3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(3-hydroxy-3-methylbut-1-ynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
10 N-Cyclopropyl-1-[3-(3-hydroxy-3-methylbut-1-ynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(1-hydroxycyclopentyl)ethynylphenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(1-hydroxycyclopropyl)ethynylphenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
15 N-Isopropyl-1-[3-[4,4,4-trifluoro-3-hydroxy-3-(trifluoromethyl)but-1-ynyl]phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(3-hydroxy-3-phenylbut-1-ynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
20 N-Cyclopropyl-1-[3-(1-oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(3-amino-3-ethylpent-1-ynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide; or  
N-Cyclopropyl-1-[3-(3-amino-3-ethylpent-1-ynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
25 N-Isopropyl-1-[3-(3-quinolinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide; or  
N-Isopropyl-1-[3-(1-oxido-3-quinolinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
30 N-Isopropyl-1-[3-(cyclopropylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-(6-amino-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
N-Isopropyl-1-[3-[5-(1-hydroxy-1-methylethyl)-1-oxido-3-pyridinylethynyl]phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;  
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N-Isopropyl-1-{3-[6-(1-hydroxy-1-methylethyl)-3-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]-naphthyridin-4-one-3-carboxamide;

N-Isopropyl-1-{3-[6-(1-hydroxy-1-methylethyl)-1-oxido-3-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

5 N-Isopropyl-1-{3-[4-(1-hydroxy-1-methylethyl)-2-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]-naphthyridin-4-one-3-carboxamide;

N-Isopropyl-1-{3-[5-(1-hydroxy-1-methylethyl)-2-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]-naphthyridin-4-one-3-carboxamide;

10 N-Isopropyl-1-{3-[6-(1-hydroxy-1-methylethyl)-2-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]-naphthyridin-4-one-3-carboxamide;

N-Cyclopropyl-1-{3-[6-(1-hydroxy-1-methylethyl)-1-oxido-3-pyridinylethynyl]phenyl}-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

N-Isopropyl-1-{3-[(4-pyridin-3-ylphenyl)ethynyl]phenyl}-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

15 N-Isopropyl-1-(3-{[5-(1-hydroxy-1-methylethyl)thien-2-yl]ethynyl}phenyl)-1,4-dihydro[1,8]-naphthyridin-4-one-3-carboxamide;

N-Isopropyl-1-(3-{[2-(1-hydroxy-1-methylethyl)-1,3-thiazol-5-yl]ethynyl}phenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

1-[3-(1-Oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide;

20 and

1-[3-(1-Oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxylic acid, or a pharmaceutically acceptable salt thereof.